PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
227/03621		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IL 03/00533	25.06.2003	25.06.2002
International Patent Classification (IPC) or both national classification and IPC		
A61B5/00		
Applicant		
GLUCON INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22.01.2004	13.09.2004
Name and mailing address of the international preliminary examining authority:	Authorized Officer
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IL 03/00533

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-19 as originally filed

Claims, Numbers

1-18 filed with telefax on 22.08.2004

Drawings, Sheets

1/9-9/9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-18
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations

see separate sheet

Reference is made to the following documents:

D1: WO 00 62659 A (SNOW BRENT W ;CARTWRIGHT PATRICK C (US); MANSFIELD JOHN T (US)) 26 October 2000 (2000-10-26)

D2: LARIN K ET AL: 'MONITORING OF TEMPERATURE DISTRIBUTION IN TISSUES WITH OPTOACOUSTIC TECHNIQUE IN REAL TIME' PROCEEDINGS OF THE SPIE, SPIE, BELLINGHAM, VA, US, vol. 3916, 25 January 2000 (2000-01-25), pages 311-321, XP008008329 ISSN: 0277-786X

D3: SEIP R ET AL: "NONINVASIVE ESTIMATION OF TISSUE TEMPERATURE RESPONSE TO HEATING FIELDS USING DIAGNOSTIC ULTRASOUND" IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, IEEE INC. NEW YORK, US, vol. 42, no. 8, 1 August 1995 (1995-08-01), pages 828-839, XP000556811 ISSN: 0018-9294

V

1. The combination of the features of claim 1 is neither known from, nor rendered obvious by, the available prior art.

   Document D1 discloses a tissue monitor comprising a heat source and means for non invasively determining the temperature development inside the tissue in order to determine tissue viability (page 5, lines 23-35). It may be obvious to use photoacoustical spectroscopy for non invasive temperature measurement as defined for example in document D2 (see abstract). However, the additional feature according to which the concentration of an analyte is also determined photoacoustically, thereby improving the accuracy of the measurement, is neither known from nor rendered obvious by, the available prior art. Thus, the subject-matter of claim 1 meets the requirements of Article 33(2)-(4) PCT.

1.1 Claims 2- 16 are dependent on claim 1 and therefore also meet the requirements of Article 33(2)-(4) PCT.

2. The combination of the features of claim 17 is neither known from, nor rendered obvious by, the available prior art.

   Document D1 discloses a tissue monitor comprising a heat source and means for non invasively determining the temperature development inside the tissue in order to determine tissue viability (page 5, lines 23-35). It may be obvious to use conventional diagnostic ultrasound for non invasive temperature measurement as defined for example in document D3 (see abstract). However, the additional

feature according to which the concentration of an analyte is determined photoacoustically, thereby improving the accuracy of the measurement, is neither known from nor rendered obvious by, the available prior art. Thus, the subject-matter of claim 17 meets the requirements of Article 33(2)-(4) PCT.

2.1 Claims 18 is dependent on claim 17 and therefore also meets the requirements of Article 33(2)-(4) PCT.

3. The independent claims should have been drafted in the two part form in accordance with Rule 6.3(b) PCT, with those features known in combination from D1 being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in a characterising part (Rule 6.3(b)(ii) PCT).

4. The features of the claims should have been provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

5. According to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D3 should have been mentioned in the description and these documents should have been identified therein.

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DT01 Rec'd PCT/PTC 22 DEC 2004

CLAIMS

1. A tissue viability monitor (TVM) for determining viability of a biological tissue comprising:

at least one light source controllable to illuminate the tissue with light that is absorbed by an analyte in the tissue to generate photoacoustic waves therein;

at least one acoustic transducer that generates signals responsive to the photoacoustic waves;

means for generating a temperature difference between temperature of the tissue and an ambient temperature of surrounding tissue; and

a controller adapted to control the means for generating a temperature difference in the tissue and to control the light source to illuminate the tissue with light absorbed by at least one analyte in the tissue and wherein the controller processes the signals generated by the at least one transducer to determine concentration of at least one analyte in the tissue and to determine temperature in the tissue and therefrom a relaxation time during which the temperature difference relaxes to zero and uses the concentration and relaxation time to provide a measure of viability.

2. A TVM in accordance with claim 1 wherein the controller processes the signals to determine locations of sources of the photoacoustic waves within the tissue.

3. A TVM in accordance with claim 2 wherein the locations of sources of photoacoustic waves are determined with a resolution equal to or better than about 100 micrometers.

4. A TVM in accordance with claim 2 wherein the locations of sources of photoacoustic waves are determined with a resolution equal to or better than about 50 micrometers.

5. A TVM in accordance with claim 2 wherein the locations of sources of photoacoustic waves are determined with a resolution equal to or better than about 20 micrometers.

6. A TVM in accordance with any of the preceding claims wherein the at least one analyte is a plurality of analytes.

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7. A TVM in accordance with any of the preceding claims wherein the at least one analyte comprises the redox state cytochrome a,a_3.

8. A TVM in accordance with any of the preceding claims wherein the at least one analyte comprises Hydrogen ions.

9. A TVM in accordance with any of the preceding claims wherein the at least one analyte comprises hemoglobin.

10. A TVM in accordance with any of the preceding claims wherein the at least one analyte comprises oxygenated hemoglobin.

11. A TVM in accordance with any of the preceding claims wherein the means for generating a temperature difference comprises an acoustic transducer, which the controller controls to transmit acoustic waves to the tissue that generate the temperature difference.

12. A TVM in accordance with any of the preceding claims wherein the controller determines temperature of the tissue during generation of the temperature difference to monitor the generation of the temperature difference.

13. A TVM in accordance with claim 12 wherein the controller controls the means for generating a temperature difference responsive to the determined temperature.

14. A TVM in accordance with any of the preceding claims wherein to determine the relaxation time the light source illuminates the tissue with light at a wavelength at which light is absorbed by water to generate photoacoustic waves in the tissue and the controller uses the signals generated by the at least one transducer to determine temperature of water in the tissue and thereby of the tissue.

15. A TVM according to any of the preceding claims and comprising a catheter having a probe end that is positioned in a neighborhood of or in contact with the tissue to determine tissue viability and wherein the light source comprises an optic fiber having an optic end located at the probe end from which optic end light that illuminates the tissue is radiated.

16. A TVM in accordance with claim 15 wherein the at least one acoustic transducer comprises at least one acoustic transducer mounted in the probe end of the catheter.

17. A tissue viability monitor (TVM) for determining viability of a biological tissue comprising:

at least one light source controllable to illuminate the tissue with light that is absorbed by an analyte in the tissue to generate photoacoustic waves therein;

at least one transmitting acoustic transducer controllable to transmit waves that are incident on the tissue;

at least one sensing acoustic transducer that generates signals responsive to the photoacoustic waves and waves from the incident waves that are reflected by the tissue;

means for generating a temperature difference between temperature of the tissue and an ambient temperature of surrounding tissue; and

a controller that processes the signals responsive to photoacoustic waves to determine concentration of at least one analyte in the tissue and the signals responsive to reflected waves to determine temperature of the tissue and therefrom a relaxation time during which the temperature difference relaxes to zero and wherein the controller uses the concentration and relaxation time to provide a measure of viability.

18. A TVM according to claim 17 wherein the characteristic is a frequency shift of the scattered acoustic waves relative to a fundamental acoustic frequency of the structure of the tissue.